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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/806,708	04/03/2001	Ljerka Kunst	4810-58741	5955

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EXAMINER	
BAUM, STUART F	

ART UNIT	PAPER NUMBER
1638	11

DATE MAILED: 06/19/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/806,708	Applicant(s) KUNST ET AL.	
	Examiner Stuart Baum	Art Unit 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 June 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7,13 and 15-25* is/are pending in the application.

4a) Of the above claim(s) *26-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,7,13 and 15-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
4) ☐ Interview Summary (PTO-413) Paper No(s) _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other

The amendment PreB filed 04 June, 2001 has been entered.

Claims 2-6, 8-12, and 14 have been cancelled.

Claims 1, 7, 13, and 15-20 have been amended.

Claims 21-28 have been added.

Claims 26-28 are withdrawn as they are drawn to non-elected material

Claims 1 and 22 are objected to for reading on non-elected material.

Claims 1, 7, 13, and 15-25 are examined in the present office action.

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in response to this action, to elect a single invention to which the claims must be restricted.

Group I claims 1, 7, 13, 15-23, 25-28 are drawn to a recombinant nucleic acid molecule comprising a heterologous promoter operably linked to a nucleic acid molecule, a transformed plant cell, and method of altering phenotype of a seed.

Applicant is to select one sequence from the list below:

A. SEQ ID NO:15
B. SEQ ID NO:16
C SEQ ID NO:17
D SEQ ID NO:18

Group II claim 24 is drawn to a method of isolating a promoter.

The claims are not linked by a single special technical feature because the invention of Group I does not constitute an advance over the prior art. Seed specific promoters of Group I are taught by Singh et al (1997, Plant Science 130:189-196) who teach seed specific promoters of rice and methods of using them. Hence, there is no special technical feature that links a recombinant nucleic acid molecule comprising a heterologous promoter operably linked to a nucleic acid molecule, a transformed plant cell, and method of altering phenotype of a seed of Group I to the method of isolating a promoter of Group II.

Applicant is reminded that nucleotide sequences either encoding different proteins or specifying specific expression patterns are structurally distinct chemical compounds and are unrelated to one another. These sequences are thus deemed to normally constitute **independent and distinct** inventions within the meaning of 35 U.S.C. 121. Absent evidence to the contrary, each such sequence is presumed to represent an independent and distinct invention, subject to a restriction requirement pursuant to 35 U.S.C. 121 and 37 CFR 1.141 et seq (see MPEP 803.04 and 2434). This requirement is not to be construed as a requirement for an election of species, since each nucleotide and amino acid sequence is not a member of a single genus of invention, but constitutes an independent and patentably distinct invention.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, fields of search, and classification, restriction for examination purposes as indicated is proper.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

During a telephone conversation with Tanya Harding on 6/4/02, a provisional election was made with traverse to prosecute the invention of Group I, claims 1, 7, 13, 15-23, and 25-28 including SEQ ID NO:15. Affirmation of this election must be made by applicant in replying to this Office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 7, 13, and 15-25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The Applicants claim a recombinant nucleic acid molecule comprising a heterologous promoter operably linked to a nucleic acid sequence wherein the promoter mediates seed-specific expression in Arabidopsis and hybridizes under stringent conditions to SEQ ID NO:15, or a

promoter sequence that is 70% or 80% identical to SEQ ID NO:15, a plant comprising said recombinant nucleic acid molecule, and a method for altering the phenotype of a seed.

The Applicants isolated their invention using the sequence information of the *Arabidopsis thaliana* sequencing project. Synthetic oligonuceotides primers were designed to amplify the *FATTY ACID ELONGATION1* (*FAE1*) gene untranslated region which generated a 934 bp fragment. The Applicants tested the 934 bp fragment along with a 393 bp, both of which conferred seed-specific expression in *Arabidopsis*.

The Applicants do not identify structural features unique to the 393 bp fragment from the *Arabidopsis FAE1* promoter of SEQ ID NO:15. The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In summary, the court stated that a written description of an invention requires a precise definition, one that defines the structural features of the chemical genus that distinguishes it from other chemical structures. A definition by function does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. Given the lack of description for the *Arabidopsis FAE1* promoter, it remains unclear what features identify a 393 bp fragment from the *Arabidopsis FAE1* promoter, including a *Arabidopsis FAE1* promoter with 70% homology to SEQ ID NO:15 or any sequence that hybridizes under stringent conditions to SEQ ID NO:15. Since a 393 bp fragment from the *Arabidopsis FAE1* promoter has not been described by specific structural features or by specific function, the specification fails to provide an adequate written description to support the generic claims.

Claims 1, 7, 13, and 15-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for claims limited to 393 bp's from the *Arabidopsis FAE1* promoter to obtain seed-specific expression of a GUS reporter gene in *Arabidopsis*, does not reasonably provide enablement for claims broadly drawn to sequences that hybridize under stringent conditions to SEQ ID NO:15, or sequences that are 70% or 80% identical to SEQ ID NO:15 and drawn to plant transformation with the exemplified or non-exemplified promoter fragment to obtain seed-specific expression. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn to a recombinant nucleic acid molecule comprising a heterologous promoter operably linked to a nucleic acid sequence wherein the promoter mediates seed-specific expression in Arabidopsis and hybridizes under stringent conditions to SEQ ID NO:15, or a promoter sequence that is 70% or 80% identical to SEQ ID NO:15, a plant comprising said recombinant nucleic acid molecule, and a method for altering the phenotype of a seed.

Non-coding nucleic acid sequences that exhibit base pair deletions, substitutions or rearrangements, and still hybridize under stringent conditions to SEQ ID NO:15, or have 70% or 80% sequence identity to SEQ ID NO:15 cannot be expected to maintain their promoter or enhancer activity. Izawa et al (1993, J. Mol. Biol. 230 :1131-1144) teach the nucleotides flanking the G-box (CACGTC) and C-box (GACGTC) hexameric cores were shown to affect protein binding activity and specificity of bZIP transcription factors (page 1132, bottom of right column; page 1134, bottom of left column). Hao, et al (1998, The J. of Biological Chemistry

273 (41): 26857-26861) investigated the binding activities of ethylene-responsive element-binding proteins (EREBP) to their cis-element GCC box (AGCCGCC). Creating base-pair substitutions within the GCC box modulates binding specificity, implying that different positions within the GCC box are important for differential binding by different EREBP's, in particular, substituting T's for the two G's eliminates binding completely (*supra*, pages 26857, abstract and 26860, left column, 2nd paragraph).

Not only are DNA sequences located 5' to the translation start site (ATG) sensitive to base changes, but in some instances, intronic regions have been shown to be necessary for proper gene expression. Busch et al (1999, Science 285:585-587) and Lohmann et al (2001, Cell 105 :793-803) teach *LEAFY* (*LFY*) and *WUSCHEL* (*WUS*), which have been shown to be transcription factors that together activate proper *AGAMOUS* (*AG*) expression, do so by binding to the second intron of the *AG* gene. A two base-pair mutation within the binding site of either *LFY* or *WUS* eliminates binding of either *LFY* or *WUS*, respectively (Busch et al (supra) page 587 left column, 2nd paragraph; Lohmann et al (supra) page 799, bottom and top of left and right columns) and changes the temporal and spatial *AG* expression pattern.

Given the unpredictability of determining the function of an isolated nucleic acid other than the 393 bp promoter fragment from the *Arabidopsis FAE1* promoter on the basis of its nucleotide sequence alone and the unpredictability of replicating the expression pattern of the 393 bp fragment of *Arabidopsis FAE1* promoter using a fragment that hybridizes under stringent conditions to SEQ ID NO:1 or a fragment that exhibits 70% or 80% sequence identity to SEQ ID NO:15, for the reasons stated above; given the lack of working examples and guidance using nucleic acid fragments other than the 393 bp fragment from the *Arabidopsis FAE1* promoter to

obtain seed-specific expression for the reasons stated above, given the state of the prior art which does not provide further guidance about 393 bp fragments from the *Arabidopsis FAE1* promoter and given the breadth of the claims which encompass a multitude of sequences that have not been exemplified, it would require undue experimentation by one skilled in the art to make and/or use the claimed invention.

Claim 19 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claim is drawn to a method of altering the phenotype of a seed comprising the nucleic acid sequence of claim 1 wherein the nucleic acid sequence is expressed during embryogenesis.

Due to the unpredictable nature of plant transformation, one of skill in the art can not reasonably generate transformed plants with a desired phenotype using a specific isolated gene. Levels of transgene expression in plants are generally unpredictable and vary between independent transformants; this variability is usually explained by differences in transgene copy number and/or integration site (Finnegan and McElroy, 1994. Bio/technology 12: 883-888 pg. 883 2nd paragraph) Eshed et al (2001, Current Biology 11:1251-1260 pg 1255 2nd paragraph) documented the phenotypes of plants transformed with the 35S CaMV promoter fused to the *KANADI1* gene, which is a gene normally expressed in tissues located on the bottom side of young developing leaves. Of the 30 plants that were transformed with the *KANADI1* gene, 23 plants developed only small narrow cotyledons and an arrested meristem, three produced a few

radialized leaves and four appeared normal. These results suggest that transforming plants with an endogenously expressed gene in regions of the plant in which it is not normally expressed produces highly unexpected and unpredictable results. For one skilled in the art, undue experimentation would be necessary to produce a plant with a desired phenotype.

Given the unpredictability of producing a plant with a specific modified phenotype, particularly by transforming a plant with the recombinant nucleic acid molecule of claim 1 wherein the nucleic acid sequence encodes an enzyme involved in lipid metabolism or using any nucleic acid molecule for the reasons stated above; and given the lack of guidance and working examples in the specification of using said recombinant nucleic acid molecule to alter the phenotype of a seed; it would require undue experimentation by one skilled in the art to practice the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 19, and 25 and all subsequent dependent claims are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite in the recitation "mediating". It is unclear how "mediating" affects seed-specific expression. The Examiner suggests the word "specifying" in place of mediating.

Claim 1, and 25 are indefinite in the recitation "stringent conditions". Applicant has not defined this term in the specification, in regards to actual conditions, and as such can be interpreted to include a multitude of nucleic acid sequences.

Claim 19 is indefinite and unclear in the recitation "under conditions". Omitting this phrase from the claim will rectify the rejection.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart Baum whose telephone number is (703) 305-6997. The examiner can normally be reached on Monday-Friday 8:30AM – 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 or (703) 305-3014 for regular communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the legal analyst, Kim Davis, whose telephone number is (703) 305-3015

Stuart Baum Ph.D.

June 13, 2002

ELIZABETH F. McELWAIN
PRIMARY EXAMINER
GROUP 1800